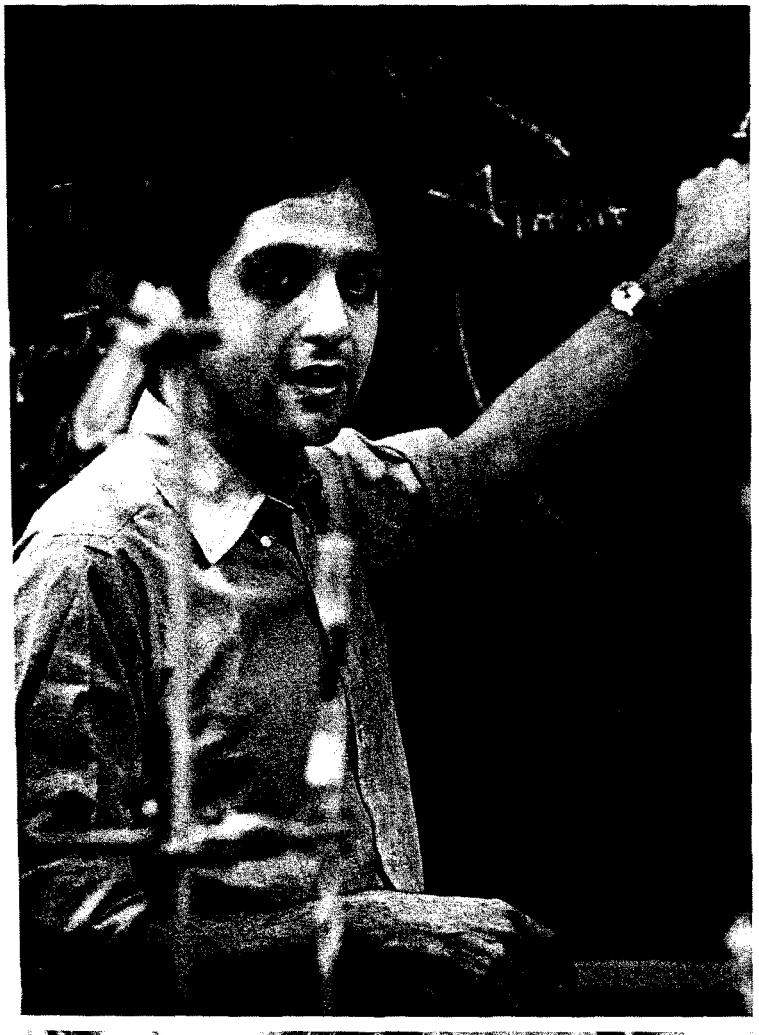
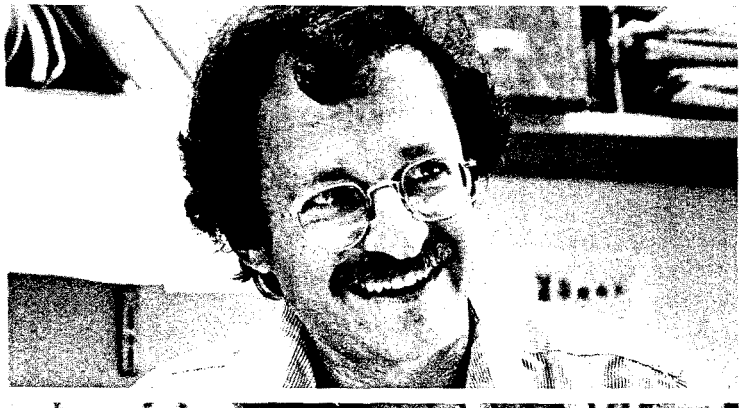
Squirrels have it





Medical explorers only recently identified the group of viruses that cause hepatitis, and they still have no cure for the disease. Although hepatitis is not new—the ancient Greek physician Hippocrates called it "infectious ikteros," after a yellow bird—the viruses are highly selective and refuse to grow in the laboratory where they might be studied.

Yet the hope of curing an illness often lies in understanding its course. By knowing the steps from onset to termination, researchers can look for a foothold against the disease's progress.

Scientists at Stanford recently found a relative of hepatitis B that thrives in squirrels. Now UCSF virologist Harold Varmus and postdocs Don Ganem and Barbara Weiser are studying a colony of infected squirrels in captivity. Early results of their study show several similarities between the squirrel and human viruses: both exist in multiple strains; both grow only in the liver; both are transmitted via blood; and both shed similar particles from the liver into the bloodstream.

By taking minute liver samples while the animals are under anesthesia, the UCSF group hopes to learn how the hepatitis-B-like squirrel virus reproduces, and how it damages the liver. The squirrels provide an unlimited supply of infected liver tissue for study; shortage of this tissue previously hampered research on human hepatitis B. Already, though, the UCSF group has discovered several novel forms of viral DNA in the squirrel liver tissue. The role these new structures play in the viral life cycle is being actively investigated. The group also is attempting to grow the squirrel virus in cell culture for further studies.

The virologists also are studying viral DNA from human hepatitis B, inserting fragments of the DNA into a type of mouse tumor cell called an L-cell. L-cells that are infected with cloned viral DNA will make small amounts of the viral coat protein. The researchers have used this system to study which regions of the viral DNA are needed for mammalian cells to produce the protein from the gene. By constructing mutants of the virus that lack parts of the viral DNA, then putting these mutant viral genes into mouse cells, the researchers can determine the specific changes that interfere with coat-protein production. Already this work has pinpointed several regions in the DNA that control the protein's synthesis. Because these control regions work similarly in all mammalian cells, the L-cell study eventually might lead to construction of a mammalian cell system that synthesizes a vaccine against hepatitis B.

Postdoc Don Ganem in Harold Varmus' tumor virology laboratory explains drawing of hepatitis B viral genome. Center, Harold Varmus. Below, squirrel in USF laboratories. Opposite page: David Altman sits at desk piled with computerized records of chronic active hepatitis patients.